(ii) at least about 80% identical to the sequence set forth in SEQ ID NO: 1047; or

(iii) encoded by a nucleic acid that hybridizes to a sequence consisting of residues 1200675 to 1199590 of SEQ ID NO: 1, under hybridization conditions that include a wash at 65°C in 0.2x SSC and 0.1% SDS.

REMARKS

With this amendment, claims 11-22 are pending in the instant application. For convenience, the Examiner's rejections are addressed in the order in which they were presented in the July 21, 2002 Office Action.

Claim 11 has been withdrawn from consideration as being directed to a non-elected invention. In the current response, Claim 11 has been amended to correct the improper presentation of SEQ ID NO:1047. This is clearly typographical error, and support for SEQ ID NO:1047 can be found on page 71, line 5 and in the fifth paragraph of the second column on page 121 (Cpn 1046), of the specification. Applicants submit that the Examiner stated that this claim was in condition for allowance in the Office Action mailed August 28, 2001.

Claim 12 has been amended to recite the functional activity of the claimed polypeptide. Support for this functional activity can be found on page 71, line 3 (Cpn 1046). In addition, claim 12 has been amended to correct a typographical error in the description of the subsequence of SEQ ID NO: 1 that encodes SEQ ID NO: 1047. Support for this amendment is found in the fifth paragraph of the second column on page 121 (Cpn 1046). In view of the foregoing support, Applicants believe no new matter has been introduced and respectfully request that claims 11-22 be entered.

Finally, applicants note that in the first paragraph of the Office Action, the Examiner has indicated that the amendment filed March 13, 2002 has been entered. Applicants understand this to refer to the amendment and other papers mailed February 28, 2002 and March 7, 2002. Applicants therefore understand that applicant's Communication mailed May23, 2002 in response to the Office Communication mailed

May 9, 2002 has been accepted as establishing that a complete response was previously submitted. If this is incorrect, applicants respectfully request clarification.

REJECTION UNDER 35 U.S.C. § 112, first paragraph:written description

Polypeptides encoded by hybridizing polynucleic acids

Claims 17-22 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide conception for the invention as now claimed, as polypeptides encoded by hybridizing polynucleic acids. Applicants understand this to be a written description rejection. In fact, written description for this invention is provided in the specification, as described below.

The present application discloses nucleic acids with hybridizing activity, see, for example, paragraphs spanning page 12, line 29 to page 18, line 6 of the application. The present application further discloses on page 21, lines 24-25, that these nucleic acids can be used for recombinant expression of proteins.

As the specification clearly supports polypeptides encoded by hybridizing polynucleic acids, withdrawal of the rejection is respectfully requested.

Claims 17-22 are also rejected under 35 U.S.C. § 112, first paragraph, based on the alleged lack of written description. The Examiner states that the claims encompass "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection further stated that "the specification provides no written description of any variants of the polypeptide that hybridize as claimed."

Applicants respectfully traverse this rejection. However, in order to expedite prosecution, the claims have been amended to incorporate a requirement of functional activity of members of the genus.

As noted in MPEP 2163.02, an objective standard for determining compliance with the written description requirement is whether the applicant conveys

with reasonable clarity to those skilled in the art that, as of the filing date of the application, he or she was in possession of the invention:

> Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim need not be described literally (i.e. using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. [emphasis added]

Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The claims set forth both a functional element, i.e. tryptophan hydroxylase activity, as well as structural elements, i.e. percent identity to a defined polypeptide reference sequence, and hybridization conditions and a reference sequence to which members of the claimed genus hybridize. Therefore, the claimed sequences are thereby defined via shared functional and structural properties.

As the claimed sequences share a defined function (i.e. enzymatic activity), polypeptide and polynucleotide variation within members of the genus is naturally limited to those sequence variations that do not interfere with the native function of the enzyme. This functional criteria of enzymatic activity for members of the genus also places an inherent requirement of structural homology upon members, e.g. conservative or a lack of variation in amino acids within the active site of the enzyme.

As the claimed sequences of the genus clearly share functional and structural properties, the members of the genus clearly meet the requirements of written description as required by the court in *Fiers v. Revel.* As such, Applicants respectfully request that the Examiner withdraw the rejection.

REJECTION UNDER 35 U.S.C. § 112, first paragraph:enablement

Claims 17-22 have also been rejected under 35 U.S.C. § 112, first paragraph, based on an alleged lack of enablement. The rejection states that the specification fails to provide enablement for 80% identical variants of SEQ ID NO:1047, or polypeptides encoded by nucleic acid sequences that hybridize to a sequence consisting of residues 1200537-1201343 of SEQ ID NO:1. The Examiner further says that the specification provides no evidence that SEQ ID NO:1047, or polynucleotide or polypeptide variants thereof, have appropriate enzymatic activity. The Examiner also says that the specification is not enabled for the nature of variation in the polynucleotide and polypeptides that would not affect activity, assay conditions to determine working diagnostic/preventive embodiments, or the use of variants for detection and diagnostic purposes.

Applicants respectfully traverse these rejections. The claims have been amended to specify enzymatic activity of the protein in addition to having a percent identity or being encoded by nucleotides having the ability to hybridize to defined nucleic acids under specified hybridization conditions. The claimed functional characteristics of the proteins encoded by the claimed nucleic acids allow one of skill in the art to identify operable embodiments and exclude inoperable embodiments. Applicants clearly meet the PTO guidelines for enablement, which set forth the standard for the scope of enablement when a large number of possible embodiments exist. Thus, undue experimentation is not required to practice the claimed invention.

The claimed reference sequences provide a meaningful structural feature permitting identification of the claimed sequences without undue experimentation.

As described above, the rejection alleges that the specification provides enablement only for the polypeptide of SEQ ID NO:1047 and the polynucleotide which encodes it. To expedite prosecution, the claims have been amended to recite additional functional characteristics of the claimed *C. pneumoniae* proteins. The present application also provides functional assays for identification of the nucleic acids and peptides of the invention, without undue experimentation. The assays and examples of the specification,

together with standard methodology known to those of skill in the art, therefore provide adequate guidance for identifying nucleic acids encoding the *C. pneumoniae* proteins of the invention.

As identified in the Patent Office and the Federal Circuit, whether undue experimentation is required by one skilled in the art to practice the invention is determined by considering factors such as the amount of guidance presented in the application, the state of the prior art, and the presence of working examples. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985); In re Wands, 8 USPQ2d 1400 (fed. Cir. 1988). As described in Wands, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." *Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982).

The present application describes a group of proteins that are defined functionally, i.e. having tryptophan hydroxylase activity, as well as structurally, i.e. have a defined percent identity to a defined amino acid sequence, or are encoded by a nucleic acid that hybridizes to a defined nucleotide sequence under clearly defined hybridization conditions.

At the time of the present invention, identification of peptides and nucleotides having the functional and structural characteristics described above was well within the means of one of skill in the art, without undue experimentation. The present application provides working examples and discloses standard techniques known to those of skill in the art, for the identification of *C. pneumoniae* proteins with tryptophan hydroxylase activity having at least 80% identity to the amino acid sequence SEQ ID NO:1047. For example, one of skill in the art could use manual or computer sequence alignment to determine whether potential *C. pneumoniae* sequences have the specified homology (see, e.g. paragraphs of the specification spanning page 6, line 19 through page 9, line 17). Additionally, one of skill in the art could use standard hybridization and PCR

assays to identify nucleic acids encoding the polypeptides of the invention (see, e.g., paragraphs of the specification spanning pages 12-21.

Finally, functional assays to identify *C. pneumoniae* proteins having tryptophan hydroxylase activity are well known in the art and the substrates and products of these assays are disclosed in the specification. For example, the specification describes tryptophan as the substrate of the tryptophan hydroxylase (see, p. 35, lines 12-15).

The assays described in the specification, coupled with methodology well known to those of skill in the art, therefore demonstrate that screening for nucleic acids encoding *C. pneumoniae* proteins described above is routine. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection be withdrawn.

One of skill in the art could readily determine any one of the claimed peptides.

Regarding the issue of enablement for nucleic acids and polypeptides, where a large number of possible embodiments exist, the PTO has provided express guidelines for examination. As set forth in the MPEP § 2164.08, a rejection of such claims such as those in the present application for undue breadth is inappropriate where one of skill could readily determine any one of the claimed embodiments.

This standard is further explained in the "Training Materials for Examining Patent Applications with respect to 35 U.S.C. § 112, first paragraph – Enablement Chemical/Biological Applications," section III A.2.b.i(c). In the guidelines, the PTO specifically answers the question regarding scope of a nucleic acid composition claim (e.g. in the present claim, a nucleic acid encoding a *C. pneumoniae* protein) left open by the Federal Circuit in *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995). The claims at issue in *Deuel* were directed to any DNA encoding a specific amino acid sequence. Thus, a great number of nucleic acids were within the scope of the claims. In fact, the number was so great that a listing of all possible DNAs encoding the protein was a practical impossibility.

In the guidelines, the PTO addressed this issue, explaining that "even though a listing of all possible DNAs which encode a given protein is a practical impossibility due to the enormous number of such nucleic acids, any particular sequence can be written by one of skill given the disclosure and the sequence can be ordered from a company which synthesizes DNA." In this manner, one of skill in the art can readily determine one of the embodiments. The PTO concluded that scope rejections such as the one hypothesized in *Deuel* should not be advanced.

In the present application, one of skill in the art has only to identify nucleic acids that encodes a protein which has tryptophan hydroxylase activity, and in which either (1) the encoded amino acid sequence has at least 80% identity to a defined reference sequence or (2) the nucleotide sequence hybridizes to a defined nucleotide sequence under specified hybridization conditions. Although many such nucleic acids are possible, one of skill can readily determine, one by one, any particular *C. pneumoniae* protein-encoding nucleic acid meeting these criteria, without undue experimentation. For example, nucleic acid screening, hybridization, and PCR techniques are described in the specification and the art, as described above. Furthermore, one of skill can use the assays described above to test the functionality of the protein encoded by the nucleic acid of interest and easily determine if it falls within the scope of the claims. Thus, in the present application the skilled artisan can readily, with only routine experimentation, make and test any particular *C. pneumoniae* protein-encoding nucleic acid meeting the defined criteria.

The specification, combined with the state of the prior art, thus provides a number of different assays demonstrating that any experimentation required to identify the claimed nucleic acids is not undue. *In re Wands*, 8 USPQ 1400 (Fed. Cir. 1988). Applicants respectfully request that the rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

Claim 17 has been rejected under 35 U.S.C. § 102(a) as being anticipated by PIR_68 Database Accession Number E72002, dated 23 April 1999, and by Griffais *et*

al. (WO 99/27105), as represented by Genseq_0601 Database Accession Number AAY35703. Applicants respectfully traverse this rejection, as the instant application claims priority to US Provisional Application No. 60/108,279, filed November 12, 1998, which precedes the publication date of both of these references. Specific support for the written description of SEQ ID NO:1047 can be found in the fourth complete paragraph of the second column, entitled CPn_1046, 1200675-1199590, Tryptophan Hyroxylase [sic], on page 95, of Provisional Application No. 60/108,279.

REJECTIONS UNDER 35 U.S.C. § 103(a)

In the Office Action, Claim 22 stands rejected for allegedly being unpatentable over Griffais *et al.* in view of Catty *et al.*. Claims 18-22 stand rejected for being allegedly unpatentable over Griffais et al. in view of PIR_68 Database Accession Number E72002, dated 23 April 1999. Claim 22 further stands rejected for allegedly being unpatentable over Griffais *et al.* in view of PIR_68 Database Accession Number E72002, dated 23 April 1999 further in view of Catty *et al.* These rejections are respectfully traversed as, as described in the previous paragraph, neither Griffais *et al.* nor PIR_68 Database Accession Number E72002 are prior art to the pending claims.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,

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PA 3240306 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

11. (Amended) An isolated [*Chlamyidia*] *Chlamydia pneumoniae* protein comprising the amino acid sequence set forth in SEQ ID NO: [1074] 1047.

12. (Amended) An isolated [*Chlamyidia*] *Chlamydia pneumoniae* protein comprising an amino acid sequence

(i) having tryptophan hydroxylase activity, and

([i]ii) at least about 80% identical to the sequence set forth in SEQ ID NO: 1047; or

(iii) encoded by a nucleic acid that hybridizes to a sequence consisting of residues [1200537 to 1201343] 1200675 to 1199590 of SEQ ID NO: 1, under hybridization conditions that include a wash at 65°C in 0.2x SSC and 0.1% SDS.